



CV TECHNOLOGIES INC.

0828 OCT 11 10:00
October 10, 2000

Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852

**RE: DOCKET NO. 00D-1392
DRAFT GUIDANCE FOR INDUSTRY ON BOTANICAL DRUG PRODUCTS,
FEDERAL REGISTER, VOL. 65, NO. 156, FRIDAY, AUGUST 11, 2000**

Dear Sir or Madam:

CV Technologies Inc., a leading Canadian Herbal Drug developer and manufacturer, appreciates the opportunity to comment on the Draft Guidance for Industry on Botanical Drug Products. CV Technologies Inc. would like to commend the FDA for the completeness and thoroughness of the draft and hopes that the comments included in this letter will assist the FDA in producing a refined guidance that will benefit both the agency and industry in developing botanical drugs. FDA's initiative to encourage the development of botanicals as licensed drugs or OTC products by publishing a specific guidance document for industry will go a long way to alleviate the confusion surrounding this category of product. While CV Technologies Inc. generally supports this draft guidance document, there are still areas for comment where we feel improvements or clarifications can be made. To this end, CV Technologies Inc.'s comments are presented following a reproduction of the text of the Guidance (in italics) below:

From I. Introduction: "In particular, the guidance states that applicants may submit reduced documentation of preclinical safety and of chemistry, manufacturing, and controls (CMC) to support an IND for initial clinical studies of botanicals that have been legally marketed in the United States as dietary supplements or cosmetics without any known safety concerns."

CV Technologies Inc. wholeheartedly supports this premise as many of the herbal products that are marketed as dietary supplements in the United States have a long history of safe use without known safety concerns. Lifting the burden of proving a compound safe when it has been on the market as a dietary supplement will allow companies to confidently move forward to prove the clinical effectiveness of their products.

... / 2

From B. CMC Information for Botanical Drug Products "For example, active constituents in a botanical drug might not need to be identified during the IND stage or in an NDA submission if this is shown to be infeasible."

CV Technologies Inc. again applauds the FDA for recognizing the complexity of developing a botanical drug based on a naturally occurring source that is more often than not of such a complex nature that it cannot be characterized in a traditional manner. However, CV Technologies Inc. is also concerned that undue burden of proof will be placed on the manufacturer to prove that the active constituents in the botanical drug being developed cannot be identified, such that it will be impossible for the manufacturer to ever comply with FDA's requirements to "show it is infeasible". CV Technologies Inc. suggests that FDA include in this section a description of the limits that will be placed on the evidence required to identify the active constituents of the botanical drug.

From B. CMC Information for Botanical Drug Products "In such circumstances, FDA will rely instead on a combination of other tests (e.g., spectroscopic or chromatographic fingerprints, chemical assay of characteristic markers, and biological assay), controls (e.g., strict quality controls of botanical raw materials and adequate in-process controls), and process validation (especially for drug substance) to ensure the identity, purity, strength, potency, and consistency of the botanical drug."

CV Technologies Inc. is pleased to see that FDA will accept other than traditional methods to define botanical drug products. However, CV Technologies Inc. is concerned that (1) the spectroscopic or chromatographic fingerprint "test" is not well defined in the guidance document and (2) the apparent need for full process validation at the IND stage. CV Technologies Inc. suggests that FDA provide a clearer definition of an acceptable fingerprint test as well as consider that full process validation for drug manufacture at the IND stage is not achievable or feasible for any drug product, including botanicals. CV Technologies Inc. believes that these issues need clarification.

From C. CMC and Toxicology Information to Support Initial Studies: "The preclinical pharmacology and toxicology information that should be provided for legally available botanical products with no known safety issues during initial clinical trials may be markedly reduced (in most cases, additional toxicology and CMC data will not be required) compared to that expected for synthetic or highly purified new drugs that are not legally marketed and for which there is no prior human experience (see 21 CFR 312.22(b))."

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CV Technologies Inc. supports FDA's proposition to reduce the amount of toxicology and CMC information for initial clinical trials of products that are legally available with no known safety issues. Additionally, CV Technologies Inc. encourages the FDA to define the types of pre-existing information that would be acceptable to support this requirement of the guidelines, in particular, what types of published data would fulfill this role.

From D. Applicability of Combination Drug Regulations "However, FDA intends to propose revisions to its regulations to allow for the exemption of such botanical drugs from application of the combination drug requirements under certain circumstances."

CV Technologies Inc. again applauds the FDA for moving forward to clarify this issue and strongly recommends to FDA that it proceed in an expeditious manner to implement this change in the legislation.

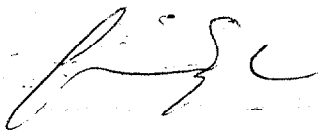
CV Technologies Inc. offers these other general comments that are applicable to the entire guidance document:

CV Technologies Inc. encourages FDA to provide appropriate educational tools to the reviewers in CDER to ensure that they fully understand the differences between botanical drugs and conventional synthetically derived drugs. The reversion to conventional synthetic drug approaches by CDER staff can be frustrating for manufacturers to deal with, especially after considerable effort may have been made to provide CDER with the appropriate information up front.

CV Technologies Inc. would also encourage the FDA to align the information in their proposed Guidance for Industry on Botanical Drug Products with that found in other standard reference materials, in particular, the United States Pharmacopoeia.

CV Technologies Inc. appreciates the opportunity to contribute to the development of this important Guidance for Industry on Botanical Drug Products. If there are any questions regarding these comments, please contact me at your convenience.

Sincerely,



JJ Jacqueline Jie Shan, Ph.D.
Senior Vice President, Research and Development



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EDMONTON, ALBERTA
CANADA

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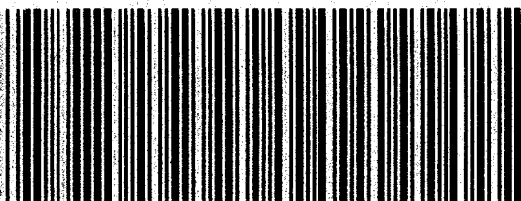
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☐ WORLDWIDE PARCEL EXPRESS
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Transport charges/Frais de transport

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☐ Sender/Expéditeur

☐ Cash/Cheque/Credit Card
Comptant/chèque/carte de crédit

For approved customers only
Pour comptes approuvés seulement

☐ External Billing Agreement
Entente de facturation extérieure

☐ Transport collect/Transport port du

Shipment insurance see reverse
Assurance sur l'envoi voir l'endos

☐ YES
OUI

Full description of contents/Description complète du contenu

PRINT MATERIAL

Country of manufacture
Pays de fabrication

International Worldwide Parcel Express shipments only/Envois Worldwide Parcel Express à destination internationale

Declared value
Valeur déclarée

Sender's VAT/GST No.
N° de TPS/TVA de l'expéditeur

Harmonised commodity code if applies
Code harmonisé de marchandises le cas échéant

Receiver's VAT/GST No. or EIN/SSN
N° de TPS/TVA ou EIN/SSN du destinataire

Type of export
Type d'exportation

☐ PERMANENT
PERMANENTE

☐ REPAIR/RETURN
REPARATION/RETOUR

☐ TEMPORARY
TEMPORAIRE

Destination duties/Taxes If left blank receiver pays duties/taxes
Droits et taxes à destination. Si vierge, le destinataire devra payer les droits et taxes.

☐ Receiver
Destinataire

☐ Sender
Expéditeur

☐ Other
Autre

Specify destination approved account number
Indiquer le numéro de compte destinataire approuvé

4 Size and weight/Taille et poids

No. of pieces
Nbre de pièces

Weight/Poids

1

.5 kg

Dimensions cm L x W x H
Dimensions cm L x L x H

VOLUMETRIC/CHARGED WEIGHT
POIDS VOLUMETRIQUE/FACTURE

kg

CODES

CHARGES/FRAIS

Services/Services

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Insurance - Assurance

Other/VAT - Autre/TVA

CURRENCY CODE
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